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EXAMINER	
HADDAD, MAHER M	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/698,121	COSGROVE, DOMINIC	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 September 2006 and 30 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-8,10-13,15,17,21,23,25,27,28 and 43-66* is/are pending in the application.

4a) Of the above claim(s) *60-66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27-28 and 43-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/21/04 and 6/30/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 9/8/06 and 6/30/06, is acknowledged.

2. Claims 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27-28 and 43-66 are pending.

3. Applicant's election with traverse of SEQ ID NO:1 species, is acknowledged.

4. Claims 60-66 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected species.

5. Claims 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27-28 and 43-59 are under consideration in the instant application as they read on a method of treating a patient having a chronic inflammatory disease with a blocking agent wherein the blocking agent is a neutralizing antibody and renal fibrosis, crescentic glomerulonephritis and SEQ ID NO: 1 as the species.

6. Applicant's IDS, filed 10/21/04 and 6/30/06, is acknowledged

7. The following new grounds of rejections are necessitated by the amendments submitted 9/8/06 and 6/30/06.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 27-28 and 48-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 27-28 and 48-52 contain the trademark name Alexa. Where a trademark name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark name is used to describe fluorescent chemicals and, accordingly, the description is indefinite.

B) Claims 27-28 and 48-52 are indefinite because it is unclear how the referenced antibodies would inhibit binding of Alexa-conjugated purified $\alpha 1\beta 1$ integrin to MCP-1 treated primary endothelial cells in vivo.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-3, 5-6, 27 and 53 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter rejection.

A. The phrase "a chronic inflammatory disease associated with the interaction of collagen XIII with $\alpha 1\beta 1$ positive monocytes" claimed in claim 1, line 2,

B. The phrase "a kidney disease associated with an accumulation of $\alpha 1\beta 1$ integrin positive monocytes in the inerstitium, the method comprising administering to the patient an antibody to collagen XIII" claimed in claim 43,

C. The phrase "a progressive renal fibrosis, the method comprising administering to the patient an antibody to collagen XIII" claimed in claim 43,

represents a departure from the specification and the claims as originally filed.

A. Applicant's amendment filed 6/30/06 points to the specification at page 2, line 30, page 9, lines 22-24 and page 10, lines 5-9 for support for the newly added limitation. However, the specification does not provide a clear support for such limitation. Obviousness is not the standard for the addition of new limitations to the disclosure as filed. It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977). The instant claims now recite limitations, which were not clearly disclosed in the specification and recited in the claims as originally filed.

B-C. Applicant's amendment filed 6/30/06 points to the specification at page 35, line 18, page 38, line 5 and page 41, line 15 for support for the newly added limitation. However, the specification does not provide a clear support for such a method using the anti-Collagen XIII antibody.

The instant claims now recite limitations, which were not clearly disclosed in the specification and recited in the claims as originally filed.

10. Claims 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27-28 and 43-59 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not reasonably provide **enablement** for a method of treating a patient having any "chronic inflammatory disease associated with the interaction of Collagen XIII with α1β1 integrin positive monocytes", the method comprising administering to the patient an antibody to Collagen XIII, wherein the antibody reduces the rate of efflux of α1β1 integrin in claim 1, wherein the chronic inflammatory disease is characterized by progressive pathogenesis resulting from infiltrating monocytes in claim 2, wherein the chronic inflammatory disease is renal fibrosis or crescentic glomerulonephritis in claim 3, or a method for treating a subject having any "inflammatory disease or other condition" where integrin α1β1-positive interstitial monocyte accumulating is observed, the method comprising administering to the subject an antibody to Collagen XIII that disrupts the interaction between Collagen XIII and α1β1 integrin in claim 7, or a method of reducing selective efflux of integrin α1β1-positive monocytes into the interstitium of chronically inflamed tissues, the method comprising contacting the α1β1 integrin on peripheral blood monocytes with an antibody to Collagen XIII that interferes with the interaction between Collagen XIII and α1β1 integrin in claim 13, or a method of reducing the rate of monocyte efflux into the interstitial space of chronically inflamed tissues, the method comprising contacting the tissue with an antibody to Collagen XIII , wherein the antibody blocks Collagen XIII from binding with α1β1 integrin in claim 17, or a method of blocking the interaction of α1β1 integrin on peripheral blood monocytes with Collagen XIII on vascular endothelium of chronically inflamed tissues, the method comprising contacting the monocytes, the vascular endothelium, or both with an antibody to Collagen XIII in claim 23, or a method of treating a patient having a kidney disease associated with an accumulation of α1β1 positive monocytes in the interstitium, the method comprising administering to the patient an antibody to Collagen XIII, wherein the antibody reduces the rate of efflux of α1β1 integrin positive monocytes into the renal interstitium in claim 43, or a method of treating a patient having a progressive renal fibrosis, the method comprising administering to the patient an antibody to Collagen XIII, wherein the antibody prevents the binding of Collagen XIII to α1β1 positive monocytes in claim 44. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

The specification fails to provide empirical data to show that method would work in vivo.

At issue, whether 1) the claimed methods would work in vivo, 2) the claimed methods would treat any chronic inflammatory disease associated with the interaction of Collagen XIII with α1β1 integrin positive monocytes, 3) the claimed method would treat a subject having an inflammatory disease or other condition where integrin α1β1-positive interstitial monocytes accumulation is observed, 4) the claimed method would reduce selective efflux of integrin α1β1-postive monocytes into the interstitium of chronically inflamed tissues, 5) the claimed method would block the interaction of α1β1 integrin on peripheral blood monocytes, 6) the claimed method would treat any kidney disease associated with an accumulation of α1β1 integrin

positive monocytes or 7) the claimed method would treat any progressive renal fibrosis.

The influence of a scientific theory should depend on its empirical and demonstrable aspects and not its underlying logic. Yet such empirical and demonstrable aspects of the claimed method of treating any inflammation, condition or kidney disease with the anti-Collagen XIII antibodies are lacked in the instant specification. No working empirical data demonstrating that the anti-Collagen XIII antibodies would treat or reduce any inflammation is disclosed. The specification provides neither working examples nor correlation between the disclosed chronic inflammatory treatment and the claimed method for treating or reducing the inflammation to establish practical methods of treating renal fibrosis or crescentic glomerulonephritis with the claimed anti-Collagen XIII antibodies. The state of the art is that current treatments of inflammation/conditions associated with the interaction of Collagen XIII with $\alpha 1\beta 1$-integrin positive monocyte, such as renal fibrosis and crescentic glomerulonephritis, is in fact unknown and untested. What are the underlying adherent and physiologic bases of the therapeutic effect of anti-Collagen XIII antibodies, which decreases the rate of efflux of $\alpha 1\beta 1$ integrin positive monocytes into the interstitial space, in the treatment of renal fibrosis or crescentic glomerulonephritis. *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

It is noted that $\alpha 1\beta 1$ integrin mediates cell spreading on collagen types I, III, IV, V and XIII, with a preference for type IV.

Although Applicant's specification describes a reduction in monocytes efflux for mice treated with a purified $\alpha 1\beta 1$ integrin. Further the specification shows that Collagen XIII immunoprecipated with purified $\alpha 1\beta 1$ integrin, Collagen XIII is induced on vascular endothelial cells from chronically inflamed kidneys and Collagen XIII and CD31 co-localized in the Alport renal cortex see pages 39-40), but their significance is unclear. Based on Collagen XIII location in tissues and cultured cells and its binding properties, Applicant concludes that the scope of the anti-Collagen XIII antibodies have biological activity to treat inflammatory disorders including renal fibrosis, crescentic glomerulonephritis or any condition associate with monocytes accumulation including kidney diseases and be provided as pharmaceutical compositions to subjects including human to effectively treat inflammatory disorders. However, there is no correlation on this record between in vitro experiments and a practical method of *in vivo* use in currently available form for humans or animals. It is not enough to rely on in vitro studies where a person having ordinary skill in the art has no basis for perceiving those studies as constituting recognized screening procedures with clear relevance to methods of *in vivo* use in humans or animals (emphasis added). Ex parte Maas, 9 USPQ2d 1746. There must be a rigorous correlation of pharmacological activity between the disclosed *in vitro* use and an *in vivo* use to establish practical methods of *in vivo* use.

Finally, the skilled medical practitioner would not be able to identify all the chronic inflammatory diseases or conditions associated with the interaction of Collagen XIII with $\alpha 1\beta 1$ integrin positive monocytes based on the disclosure.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27-28 and 43-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 99/61040 (of record) in view of Nykvist *et al* (JBC 275(11):8255-8261, 2000), U.S. Pat. No. 5,567,440 and Lin *et al* (Development 128, 1573-1585 (2001)).

The WO `040 publication teaches and claims a of treating renal fibrosis or crescentic glomerulonephritis (chronic inflammatory diseases of the kidney), in a patient comprising administering to the patient an effective amount of an $\alpha 1\beta 1$ integrin receptor inhibitor (a blocking agent) (see published claims 1 and 12-13 in particular), wherein the $\alpha 1\beta 1$ integrin receptor inhibitor is a blocking agent that binds to the $\alpha 1\beta 1$ integrin receptor binding site on the surface of a kidney cell (see published claim 8, in particular), wherein the agent is an antibody (see published claim 11 and Example 5 on page 53 in particular).

The claimed invention differs from the `040 publication teachings only by the recitation of antibody to Collagen XIII in claims 1, 7, 13, 17, 23,43, wherein the antibody is a monoclonal antibody in claims 5, 10, 21, 25, 45, wherein the antibody binds to a peptide fragment of collagen XIII having SEQ ID NO: 1 in claims 53-59.

Nykvist et al teach that $\alpha 1\beta 1$ integrin mediates cell adhesion to type XIII collagen (see abstract in particular).

The `440 patent teaches that cell adhesion plays an important role in human disease. These interactions proceed by the interaction of receptors upon the surface of a cell with proteins or glycosaminoglycans upon the surface of another cell or within the extracellular matrix. The `440

patent further teaches that routes to the interruption of these interactions typically involve competitive inhibition of these receptor-ligand interactions, for example, with antibodies, soluble ligands which act as receptor antagonists, soluble receptors, or other competitors (see col., 1 lines 17-30 in particular).

Lin et al teaches two collagen type XIII blocking monoclonal antibodies, ELQ and Q36.4 (abstract and page 1574, 2nd col., 1st full ¶ in particular).

Given that Lin's et al antibodies are blocking antibodies, the limitations recited in claims 6, 8, 12, 15, 27, 28, 46, 47-52 would be expected properties of the Lin's et al antibodies in absence of evidence to the contrary.

The term "having" in claims 53-59 would open up the claims to include the antibodies that bind to the Collagen type XIII (the full length collagen type XIII minus one amino acid).

Given Nykvist *et al* teachings that $\alpha 1\beta 1$ integrin mediates cell adhesion to type XIII collagen. Further, given the fact that routes to the interruption cell adhesion interactions typically involve competitive inhibition of these receptor-ligand interactions with either receptor antagonists, antibodies or other competitors, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the $\alpha 1\beta 1$ integrin receptor inhibitor such as an antibody taught by the `040 publication with anti-collagen type XIII antibody taught by Lin *et al.*

Further, a person of ordinary skill in the art would have recognized the interchangeability of the element shown in the prior art for the corresponding anti-collagen type XIII blocking antibodies recited in the claim. *Caterpillar Inc. v. Deere & Co.*, 224 F.3d 1374, 56 USPQ2d 1305 (Fed. Cir. 2000); *Al-Site Corp. v. VSI Int' l, Inc.*, 174 F.3d 1308, 1316, 50 USPQ2d 1161, 1165 (Fed. Cir. 1999); *Chiuminatta Concrete Concepts, Inc. v. Cardinal Indus. Inc.*, 145 F.3d 1303, 1309, 46 USPQ2d 1752, 1757 (Fed. Cir. 1998); *Lockheed Aircraft Corp. v. United States,* 193 USPQ 449, 461 (Ct. Cl. 1977*); Data Line Corp. v. Micro Technologies, Inc.*, 813 F.2d 1196, 1 USPQ2d 2052 (Fed. Cir. 1987).

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. Claims 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27-28 and 43-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Pat. No. 6,492,325 (of record) in view of Nykvist *et al* (JBC 275(11):8255-8261, 2000), U.S. Pat. No. 5,567,440 and Lin *et al* (Development 128, 1573-1585 (2001)).

The `325 patent teaches and claims a of treating renal fibrosis or crescentic glomerulonephritis (chronic inflammatory diseases of the kidney), in a patient comprising administering to the patient an effective amount of an α1β1 integrin receptor inhibitor (a blocking agent) (see patented claims 1 and col., 5, lines 40-55 in particular), wherein the α1β1 integrin receptor inhibitor is a blocking agent that binds to the α1β1 integrin receptor binding site on the surface of a kidney cell (col., 5, lines 51-55 in particular), wherein the agent is an antibody, other agents that inhibit the α1β1 integrin receptor by other mechanisms can also be use (see col., 5, lines 58-61 and col., 32 under Example 5 in particular).

The claimed invention differs from the `325 patent teachings only by the recitation of antibody to Collagen XIII in claims 1, 7, 13, 17, 23, 43, wherein the antibody is a monoclonal antibody in claims 5, 10, 21, 25, 45, wherein the antibody binds to a peptide fragment of collagen XIII having SEQ ID NO: 1 in claims 53-59.

Nykvist *et al* teach that α1β1 integrin mediates cell adhesion to type XIII collagen (see abstract in particular).

The `440 patent teaches that cell adhesion plays an important role in human disease. These interactions proceed by the interaction of receptors upon the surface of a cell with proteins or glycosaminoglycans upon the surface of another cell or within the extracellular matrix. The `440 patent further teaches that routes to the interruption of these interactions typically involve competitive inhibition of these receptor-ligand interactions, for example, with antibodies, soluble ligands which act as receptor antagonists, soluble receptors, or other competitors (see col., 1 lines 17-30 in particular).

Lin et al teach two collagen type XIII blocking monoclonal antibodies, ELQ and Q36.4 (abstract and page 1574, 2nd col., 1st full ¶ in particular).

Given that Lin's et al antibodies are blocking antibodies, the limitations recited in claims 6, 8, 12, 15, 27, 28, 46, 47-52 would be expected properties of the Lin's et al antibodies in absence of evidence to the contrary.

The term "having" in claims 53-59 would open up the claims to include the antibodies that bind to the Collagen type XIII (the full length collagen type XIII minus one amino acid).

Given Nykvist *et al* teachings that α1β1 integrin mediates cell adhesion to type XIII collagen. Further, given the fact that routes to the interruption cell adhesion interactions typically involve competitive inhibition of these receptor-ligand interactions with either receptor antagonists, antibodies or other competitors, it would have been obvious to one of ordinary skill in the art at

the time the invention was made to substitute the α1β1 integrin receptor inhibitor such as an antibody taught by the '325 patent with anti-collagen type XIII antibody taught by Lin *et al.*

Further, a person of ordinary skill in the art would have recognized the interchangeability of the element shown in the prior art for the corresponding anti-collagen type XIII blocking antibodies recited in the claim. *Caterpillar Inc. v. Deere & Co.*, 224 F.3d 1374, 56 USPQ2d 1305 (Fed. Cir. 2000); *Al-Site Corp. v. VSI Int' l, Inc.*, 174 F.3d 1308, 1316, 50 USPQ2d 1161, 1165 (Fed. Cir. 1999); *Chiuminatta Concrete Concepts, Inc. v. Cardinal Indus. Inc.*, 145 F.3d 1303, 1309, 46 USPQ2d 1752, 1757 (Fed. Cir. 1998); *Lockheed Aircraft Corp. v. United States,* 193 USPQ 449, 461 (Ct. Cl. 1977*); Data Line Corp. v. Micro Technologies, Inc.*, 813 F.2d 1196, 1 USPQ2d 2052 (Fed. Cir. 1987).

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claims 1-3, 5-8, 10-13, 15, 17, 21, 23, 25, 27-28 and 43-59 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 25, 34-36, 40, 43-45, 52 of copending Application No. 10/099,573 in view of Nykvist *et al,* U.S. Pat. No. 5,567,440 and Lin *et al.*

The `573 application claims a method of limiting renal fibrosis in a patient comprising reducing TGF-b1 activity in the patient while inhibiting $\alpha 1\beta 1$ integrin receptors of patient's kidney cells (see pending claim 25). Further the `573 application claims a method of delaying the onset of and/or slowing the progression of kidney disease in a patient, the method comprising administering to the patient an effective amount of an $\alpha 1\beta 1$ integrin receptor inhibitor (pending claim 34), wherein the $\alpha 1\beta 1$integrin receptor inhibitor comprises a peptide in claim 35, wherein $\alpha 1\beta 1$integrin receptor inhibitor is an antibody in claim 36. The `573 application further claims a method of synergistically delaying the onset of and/or slowing the progression of kidney disease in a patient, the method comprising administering to the patient an $\alpha 1\beta 1$ integrin receptor inhibitor in claim 43, wherein the $\alpha 1\beta 1$integrin receptor inhibitor comprising a peptide in claim 44, wherein the $\alpha 1\beta 1$ integrin receptor inhibitor is an antibody in claim 45.

The claimed invention differs from the `573 application teachings only by the recitation of antibody to Collagen XIII in claims 1, 7, 13, 17, 23, 43, wherein the antibody is a monoclonal antibody in claims 5, 10, 21, 25, 45, wherein the antibody binds to a peptide fragment of collagen XIII having SEQ ID NO: 1 in claims 53-59.

Nykvist *et al* teach that $\alpha 1\beta 1$ integrin mediates cell adhesion to type XIII collagen (see abstract in particular).

The `440 patent teaches that cell adhesion plays an important role in human disease. These interactions proceed by the interaction of receptors upon the surface of a cell with proteins or glycosaminoglycans upon the surface of another cell or within the extracellular matrix. The `440 patent further teaches that routes to the interruption of these interactions typically involve competitive inhibition of these receptor-ligand interactions, for example, with antibodies, soluble ligands which act as receptor antagonists, soluble receptors, or other competitors (see col., 1 lines 17-30 in particular).

Lin et al teaches two collagen type XIII blocking monoclonal antibodies, ELQ and Q36.4 (abstract and page 1574, 2nd col., 1st full ¶ in particular).

Given that Lin's et al antibodies are blocking antibodies, the limitations recited in claims 6, 8, 12, 15, 27, 28, 46, 47-52 would be expected properties of the Lin's et al antibodies in absence of evidence to the contrary.

The term "having" in claims 53-59 would open up the claims to include the antibodies that bind to the Collagen type XIII (the full length Collagen XIII minus one amino acid).

Given Nykvist *et al* teachings that α1β1 integrin mediates cell adhesion to type XIII collagen. Further, given the fact that routes to the interruption cell adhesion interactions typically involve competitive inhibition of these receptor-ligand interactions with either receptor antagonists, antibodies or other competitors, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the α1β1 integrin receptor inhibitor such as an antibody taught by the `573 application with anti-collagen type XIII antibody taught by Lin *et al.*

Further, a person of ordinary skill in the art would have recognized the interchangeability of the element shown in the prior art for the corresponding anti-collagen type XIII blocking antibodies recited in the claim. *Caterpillar Inc. v. Deere & Co.*, 224 F.3d 1374, 56 USPQ2d 1305 (Fed. Cir. 2000); *Al-Site Corp. v. VSI Int' l, Inc.*, 174 F.3d 1308, 1316, 50 USPQ2d 1161, 1165 (Fed. Cir. 1999); *Chiuminatta Concrete Concepts, Inc. v. Cardinal Indus. Inc.*, 145 F.3d 1303, 1309, 46 USPQ2d 1752, 1757 (Fed. Cir. 1998); *Lockheed Aircraft Corp. v. United States,* 193 USPQ 449, 461 (Ct. Cl. 1977*); Data Line Corp. v. Micro Technologies, Inc.*, 813 F.2d 1196, 1 USPQ2d 2052 (Fed. Cir. 1987).

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.
This is a provisional obviousness-type double patenting rejection.

16. No claim is allowed.

17. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad whose telephone number is (571) 272-0845. The examiner can normally be reached Monday through Friday from 7:30 am to 4:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

October 4, 2006

Maher Haddad

Maher Haddad, Ph.D.
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